REMARKS/ARGUMENTS

Claims 1, 2, 6-8, 11, 12, and 14-17 are pending in the above-identified application. All claims currently stand rejected as allegedly unpatentable under 35 U.S.C. § 103. Reconsideration and withdrawal of these rejections are respectfully requested in view of the remarks and arguments set forth below.

Rejections Under 35 U.S.C. §103(a)

Claims 1, 2, 6, 11, 12 and 14-17

Claims 1, 2, 6, 11, 12 and 14-17 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Corr *et al.* (*J. Exp. Med.* 184:1555-1560, 1996; hereinafter "Corr (1996)") in view of Corr *et al.* (*J. Immunol.* 159:4999-5004, 1997; hereinafter "Corr (1997)"). According to the Examiner, Corr (1996) teaches IM injection of a viral protein antigen mixed with naked plasmid DNA encoding B7.1 or B7.2. While acknowledging that Corr (1996) does not teach separate administration of protein antigen and plasmid DNA encoding B7.1 or B7.2 to closely adjacent sites, it is essentially the Examiner's position that Corr (1997) provides this teaching. According to the Examiner, Corr (1997) teaches that "co-expression of B7-1 in the vicinity of a minimal MHC class I-restricted antigen is sufficient to prime a CTL response," and further teaches "IM or intradermal injection of protein antigen mixed with plasmid DNA encoding B7.1 or B7.2." (Office Action at p. 2.) The Examiner further states, *inter alia*, the following with respect to Corr (1997):

> Corr *et al* (1997) teach that expression of the MHC class I restricted epitope in the same cell as the costimulatory ligand is not imperative for T cell priming, but *in vivo* a T cell cannot be effectively primed with a cognate signal from a peripheral somatic tissue if a second signal stimulus is not available in the immediate vicinity, for example in the same muscle.
>
> [Office Action at p. 2.]

On this basis, the Examiner contends that it would have been *prima facie* obvious to have "administered the viral protein antigen taught by Corr *et al* (1996) or the CTL peptide epitope taught by Corr *et al* (1997) ***separately*** from the naked plasmid DNA encoding B7.1 and/or B7.2 co-stimulatory molecule to ***closely adjacent sites*** as taught by Corr *et al* (1997). (*Id.* at p. 3 (emphasis provided.) The Examiner states that a motivation to do so is provided by the following:

> (1) "because co-administration or separate administration to closely adjacent sites are equivalent methods";
>
> (2) "because the same naked plasmid DNA preparation administered separately to a closely adjacent site could be used for co-ordinate immunizations with different protein or peptide antigens"; and
>
> (3) "because Corr *et al* (1997) teach that co-expression of B7-1 in the vicinity of a minimal MHC class I-restricted antigen is sufficient to prime a CTL response, including wherein the antigen is a protein antigen."
>
> [Office Action at p. 3.]

Applicants traverse the instant rejection. It is submitted that Corr 1996 and Corr 1997 do not render the present claims *prima facie* obviousness because, contrary to the Examiner's assertions, these references do not teach or suggest "separate administration to closely adjacent sites," nor do these references provide a sufficient motivation to achieve this limitation as recited in the claims, for the reasons discussed further below.

First, as indicated in Applicants' previous responses, a *prima facie* case of obviousness requires, *inter alia*, that all claim limitations be taught or suggested by the prior art. Such a showing has not been made in this case. As note above, the Examiner acknowledges that Corr 1996 does not teach separate administration of protein antigen and plasmid DNA to closely adjacent sites, but rather appears to rely on Corr 1997 for such a showing. In particular, the Examiner states the Corr 1997 teaches "co-expression of B7-1 in the vicinity of a minimal MHC class I-restricted antigen is sufficient to prime a CTL response." Corr 1997, however, does ***not*** show separate administration of protein antigen and B7-encoding DNA to closely adjacent sites.

Instead, the only study in Corr 1997, in which protein antigen and B7-encoding plasmid were administered so as to elicit an immune response, utilized a mixture of protein antigen and plasmid. (*See* Corr 1997 at, *e.g.*, p. 5002, Figure 5 legend (discussing i.m. injection of mice "with 10 μg of OVA mixed with 50 μg of ... plasmid" (emphasis provided)).) For at least these reasons, not all claim limitations have been shown in the prior art and, therefore, a *prima facie* case obviousness has not been established.

Second, the Examiner has not shown a sufficient motivation to combine Corr 1996 and Corr 1997 so as to achieve the invention as presently claimed. As discussed in Applicants' previous response, a suggestion or motivation to make the claimed combination must be found in the prior art and cannot be based on applicant's disclosure. *See* MPEP § 2142. *See also* MPEP §§ 2143 and 2143.01 (citing cases). The proposed motivation must have sufficient "force" to "impel persons skilled in the art to do what applicant has done." *Ex parte Levengood,* 28 USPQ2d 1300, 1302 (Bd. Pat. App. Inter. 1993). Moreover, the motivation must be both objective and specific, *i.e.*, the Examiner's showing must be clear and particular. *See In re Dembiczak*, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999). It is this requirement for evidence of particularized motivation that provides a safeguard against the "tempting but forbidden zone of hindsight." *Id.* at 1616.

In this case, none of the Examiner's proposed motivations meet all of the above criteria and are thus insufficient to establish a *prima facie* case under 35 U.S.C. § 103. With respect to the Examiner's assertion that "co-administration or separate administration to closely adjacent sites are equivalent methods," the Examiner has not shown such a teaching in the prior art itself. As noted above, Corr 1997 demonstrates elicitation of an immune response only with a mixture of protein antigen and plasmid. If the Examiner wishes to rely on an alleged knowledge in the prior art of an equivalency of co-administration and separate administration to closely adjacent sites, it is respectfully requested that the Examiner point to a showing of this knowledge in the prior art or submit an affidavit testifying that such equivalency was common knowledge in the art as of the application's filing date.

As to the Examiner's statement that a motivation is provided because "the same naked plasmid DNA preparation administered separately to a closely adjacent site could be used for co-ordinate immunizations with different protein or peptide antigens," once again, the Examiner has not pointed to a teaching of this advantage in the prior art itself, as required for any analysis of motivation under 35 U.S.C. § 103. Once again, Applicants respectfully request that the Examiner show evidence of such knowledge in the prior art, either in a reference or by affidavit.

With respect to the Examiner's reliance on Corr (1997) as teaching "that co-expression of B7-1 in the vicinity of a minimal MHC class I-restricted antigen is sufficient to prime a CTL response, including wherein the antigen is a protein antigen," Applicants again note that Corr (1997) only demonstrates an immune response only when protein antigen and B7-encoding DNA are co-administered as a mixture. Accordingly, when the disclosure of Corr 1997 is viewed objectively, without the benefit of hindsight in view of Applicants' specification, Corr 1997 does not provide any clear and particular motivation to achieve separate administration to closely adjacent sites as presently claimed.

For at least the reasons above, a *prima facie* case of obviousness in view of Corr (1996) and Corr (1997) has not been established with respect to the present claims. Withdrawal of the present rejection is respectfully requested.

Claims 7 and 8

Claims 7 and 8 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Corr (1996) in view of Corr (1997) as applied to claims 1, 2, 6, 11, 12 and 14-17, and further in view of WO 99/45954 A1. Essentially, the Examiner relies on WO 99/45954 as allegedly teaching or suggesting the antigens as recited in claims 7 and 8, and states that it would have been prima facie obvious to combine the teaching of WO 99/45954 with those of Corr (1996) and Corr (1997) to achieve the invention as in claims 7 and 8.

This rejection is traversed for at least the reasons set forth above with respect to claims 1 and 2, from which claims 7 and 8 depend. It is noted that WO 99/45954 does not cure the deficiencies of Corr (1996) and Corr (1997) with respect to any teaching or suggestion of separate administration of protein antigen and a non-viral vector comprising a polynucleotide sequence encoding B7 to closely adjacent sites. Accordingly, a combination of WO 99/45954 with the Corr references is also insufficient to render claims 7 and 8 obvious under 35 U.S.C. § 103. Withdrawal of the rejection is therefore respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.

Respectfully submitted,

Dated: March 15, 2007

Nicholas V. Sherbina
Reg. No. 54,443

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 206-467-9600
Fax: 415-576-0300
NVS:jae
60933003 v1